REMARKS/ARGUMENTS

Upon entry of this amendment, claims 1-9 and 11-16 will be amended, whereby claims 1-16 will remain pending. Claim 1 is the sole independent claims.

Support for the amendments to the claims appears throughout Applicants' originally filed application, including Applicants' specification beginning at page 16 and Applicants' specification beginning at the bottom of page 255. Moreover, attention is directed to Compound No. XB169 wherein Y is a hydroxyl group, and Compound Nos. XA1649, YA1339 and YA1341 where Y is a C1-C8 alkyl group.

Reconsideration and allowance of the application are respectfully requested.

Information Disclosure Statement

Applicants are submitting herewith an Information Disclosure Statement. The Examiner is requested to indicate consideration of this Information Disclosure Statement by including an initialed copy of the Form PTO-1449 submitted therewith with the next communication from the Patent and Trademark Office.

Claim Of Priority

Applicants express appreciation for the acknowledgement of the claim of foreign priority as well as receipt of the certified copy of the priority application. In this regard, Applicants note that the box on the Cover Sheet of the Office Action, Form PTOL-326 should indicate that the certified copy has been received in this National Stage application from the International Bureau.

Response To Rejection Under 35 U.S.C. 112, Second Paragraph

In response to the rejection of claims 11-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite, Applicants respectfully submit the following.

By the amendment herein, claim 11 has been amended to even more clearly recite a medicament composition; and claims 12-16 have been amended to be directed to methods including positive recitation of method steps.

Accordingly, the 35 U.S.C. 112, second paragraph, rejection should be withdrawn.

Response To Rejection Under 35 U.S.C. 112, First Paragraph

In response to the rejection of claims 1-16 under 35 U.S.C. 112, first paragraph, as the Examiner asserts that the specification, while being enabling for making pharmaceutically acceptable salts does not reasonable provide enablement for making solvate or hydrate thereof, Applicants respectfully submit the following.

The Examiner is reminded that working examples are not required. The rejection must provide clear technical reasoning to support a lack of enablement for solvates and hydrates, instead of merely pointing to documents that have disclosures broadly relating to compounds and their solvates and hydrates. In any event, in order to advance prosecution of the application, without expressing any agreement or acquiescence with the rejection of record, the claims have been amended to delete solvates and hydrates. Accordingly, this ground of rejection should be withdrawn.

Response To Rejection Under 35 U.S.C. 101

In response to the rejection of claims 13-16 under 35 U.S.C. 101 as being directed to a use, Applicants respectfully submit the following.

As discussed above by the amendment herein, claims 13-16 been amended to be directed to methods including positive recitation of method steps.

Accordingly, the 35 U.S.C. 101 rejection should be withdrawn.

Response To 35 U.S.C. 103(a) Rejection Over EP 1136482

In response to the rejection of claims 1-5, 8, 9 and 11-16 under 35 U.S.C. 103(a) as being unpatentable over Almario-Garcia et al., EP 1136482 (hereinafter "Almario-Garcia"), Applicants respectfully submit the following.

In this ground of rejection, the Examiner is contending that Almario-Garcia differs from the rejected claims in not exemplifying compounds wherein R^1 and R^2 form a ring. The rejection contends that it would have been obvious to have compounds in Almario-Garcia wherein R^1 and R^2 form a ring.

Applicants submit that one having ordinary skill in the art would not have been motivated to arrive at Applicants' claimed subject matter from the disclosure of Almario-Garcia. Applicants therefore respectfully submit that the rejection does not set forth a *prima facie* case of obviousness and the rejection should be withdrawn for at least this reason.

Moreover, the compounds of the present invention have more potent TPK1 inhibitory activity compared to that of the compounds disclosed in of Almario-Garcia. As is disclosed at page 15, lines 53 and 54 of Almario-Garcia, GSK3β (=TPK1) inhibitory activities of the compounds disclosed in Almario-Garcia, which are expressed in IC50 values, are between 0.1 to 10 micromolar concentrations (= 100 to 10,000 nM).

Applicants are submitting herewith a Declaration Under 37 C.F.R. 1.132 by one of the inventors, Dr. Kazutoshi Watanabe, referring to experiments to show the inhibitory activity of Compounds 38 and 39 of Almario-Garcia, as compared to compounds of the present invention

against P-GS1 phosphorylation by bovine cerebral TPK1. In this regard, Compound Nos. 38 and 39 appear to be the closest compounds to Applicants' claimed subject matter.

The Examiner is referred to the Declaration referring to Compound Nos. 38 and 39 of Almario-Garcia and the Table attached to the Declaration for comparison of the compounds according to the present invention as compared to comparative compounds of Almario-Garcia which are revealed to have much lower inhibitory activity. As shown in the Declaration, Compound Nos. 38 and 39 of Almario-Garcia have IC_{50} values of >1000 nM. In contrast, compounds according to the present invention have TPK1 inhibitory activities between 0.25 to 43 nM. Applicants submit that these results are unexpected by one of ordinary skill in the art.

Accordingly, for this additional reason, the rejection of record should be withdrawn.

Response To Obviousness Type Double Patenting Rejections

(a) Claims 1-11 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 3 of U.S. Patent No. 6,844,335.

In compounds recited in claims 1 and 3 of in U.S. Patent No. 6,844,335, R1 and R2 can form together a C2-6 alkylene group which may be substituted, resulting in formation of a ring substituted at 2-position of the pyrimidone ring. Consequently, the compounds represented by formula (I) in U.S. Patent No. 6,844,335 could form a compound similar to the compounds of the present invention. The specifically disclosed compounds which fall within the above definition of R1 and R2 are only compounds No.38 and No.39 on columns 23 and 24. However, compounds No.38 and No.39 have no substituent on the ring which is formed by R1 and R2. In contrast, the compounds of the present invention have essentially a substituted piperazine ring or a substituted piperidine ring at 2-position of the pyrimidone ring. Having such structure, the compounds of the

present invention achieve more potent TPK1 inhibitory activity as discussed above with respect to the rejection under 35 U.S.C. 103 (a).

Applicants therefore respectfully request withdrawal of the present rejection.

Moreover, in order that the record is complete, Applicants note that U.S. Patent No. 6,844,335 is a national stage of PCT/EP01/03640, which published as WO 01/70729 A1 on September 27, 2001.

(b) Claims 1-16 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-25 of copending application No. 10/489,606.

In the compounds represented by formula (I) in the claims of U.S. Patent Application No. 10/489,606, R present at 2-position of the pyrimidone ring can be formula (IV) forming piperidine or piperazine, or formula (V) forming piperidine, both of which could form a compound similar to the compounds of the present invention. However, the disclosed compounds which are included in the above definition essentially have a substituent having carbonyl group (-CO-R9 or —CO-R10). In contrast, the substituted piperazine ring or substituted piperidine ring at 2-position of the pyrimidone ring of the compounds of the present invention do not include substituents structurally having carbonyl group. Therefore, the compounds of the present invention are different from the compounds recited in 10/489,606.

Accordingly, this ground of rejection should be withdrawn.

Moreover, in order that the record is complete, Applicants note that U.S. Patent Application No. 10/489,606 is a national stage of PCT/JP02/09685, which published as WO 03/037888 A1 on May 8, 2003.

(c) Claims 1-16 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-25 of copending application No. 10/489,607.

Applicants note that the same comments apply to this ground of rejection as that for U.S. Patent Application No. 10/489,606. Thus, in the compounds represented by formula (I) in the claims of U.S. Patent Application No. 10/489,607, R present at 2-position of the pyrimidone ring can be formula (IV) forming piperidine or piperazine, or formula (V) forming piperidine, both of which could form a compound similar to the compounds of the present invention. However, the disclosed compounds which are included in the above definition essentially have a substituent having carbonyl group (-CO-R9 or —CO-R10). In contrast, the substituted piperazine ring or substituted piperidine ring at 2-position of the pyrimidone ring of the compounds of the present invention do not include substituents structurally having carbonyl group. Therefore, the compounds of the present invention are different from the compounds recited in 10/489,607.

Accordingly, this ground of rejection should be withdrawn.

Moreover, in order that the record is complete, Applicants note that U.S. Patent Application No. 10/489,607 is a national stage of PCT/JP02/09684, which published as WO 03/027080 A1 on April 3, 2003.

(d) Claims 1-16 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-25 of copending Application No. 11/035,264.

Initially, Applicants note that this application is a divisional application of the U.S. 6,844,335 utilize in the rejection discuss above.

In the compound represented by formula (I) in U.S. Patent Application No. 11/035,264, R1 and R2 can bind to form together $-(CH_2)_2$-X-$(CH_2)_2$- or $-(CH_2)_2$-X-$(CH_2)_3$- (wherein X represents oxygen atom, sulfur atom, or nitrogen atom) which may be substituted. When X is nitrogen atom, the disclosed compound could form a compound similar to the compounds of the present invention. However, neither specific compounds which fall within the above definition of

R1 and R2 nor their pharmacological activity are specifically disclosed in the specification of this application.

Applicants respectfully submit that the present claims are not rendered obvious by U.S. Patent Application No. 11/035,264. Accordingly, this ground of rejection should be withdrawn.

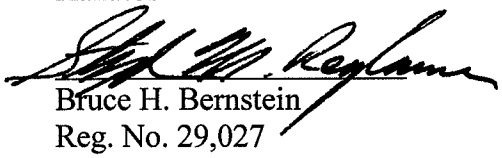
CONCLUSION

In view of the foregoing, the Examiner is respectfully requested to reconsider and withdraw the rejections of record, and allow each of the pending claims.

Applicants therefore respectfully request that an early indication of allowance of the application be indicated by the mailing of the Notices of Allowance and Allowability.

Should the Examiner have any questions regarding this application, the Examiner is invited to contact the undersigned at the below-listed telephone number.

Respectfully submitted,
Kazutoshi WATANABE et al.



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